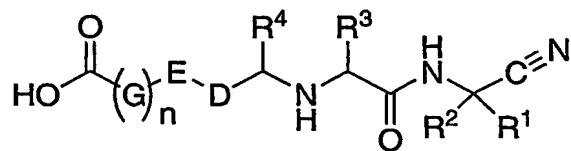


## WHAT IS CLAIMED IS:

1. The present invention relates to compounds of the following chemical formula:



- 5 wherein R<sup>1</sup> is hydrogen, C<sub>1-6</sub> alkyl or C<sub>2-6</sub> alkenyl wherein said alkyl and alkenyl groups are optionally substituted with one to six halo, C<sub>3-6</sub> cycloalkyl, -SR<sup>5</sup>, -SOR<sup>5</sup>, -SO<sub>2</sub>R<sup>5</sup>, -SO<sub>2</sub>CH(R<sup>a</sup>)(R<sup>b</sup>), -OR<sup>5</sup>, -N(R<sup>5</sup>)<sub>2</sub>, aryl, heteroaryl or heterocyclyl wherein said aryl, heteroaryl and heterocyclyl groups are optionally substituted with one or two substituents independently selected from the group consisting of C<sub>1-6</sub> alkyl, halo, hydroxyalkyl, hydroxy, alkoxy and keto;
- 10 R<sup>2</sup> is hydrogen, C<sub>1-6</sub> alkyl or C<sub>2-6</sub> alkenyl wherein said alkyl and alkenyl groups are optionally substituted with one to six halo, C<sub>3-6</sub> cycloalkyl, -SR<sup>5</sup>, -SOR<sup>5</sup>, -SO<sub>2</sub>R<sup>5</sup>, -SO<sub>2</sub>CH(R<sup>a</sup>)(R<sup>b</sup>), -OR<sup>5</sup>, -N(R<sup>5</sup>)<sub>2</sub>, aryl, heteroaryl or heterocyclyl wherein said aryl, heteroaryl and heterocyclyl groups are optionally substituted with one or two substituents independently selected from the group consisting of C<sub>1-6</sub> alkyl, halo, hydroxyalkyl, hydroxy, alkoxy and keto;
- 15 or R<sup>1</sup> and R<sup>2</sup> can be taken together with the carbon atom to which they are attached to form a C<sub>3-8</sub> cycloalkyl or heterocyclyl ring wherein said ring system is optionally substituted with one or two substituents independently selected from the group consisting of C<sub>1-6</sub> alkyl, hydroxyalkyl, haloalkyl, or halo;
- 20 R<sup>3</sup> is hydrogen, C<sub>1-6</sub> alkyl or C<sub>2-6</sub> alkenyl wherein said alkyl and alkenyl groups are optionally substituted with C<sub>3-6</sub> cycloalkyl or one to six halo;
- R<sup>4</sup> is hydrogen or C<sub>1-6</sub> alkyl substituted with 1-6 halo;
- 25 D is aryl or heteroaryl, wherein said aryl or heteroaryl group, which may be monocyclic or bicyclic, is optionally substituted on either the carbon or the heteroatom with one to five substituents independently selected from the group consisting of C<sub>1-6</sub> alkyl, haloalkyl, halo, keto, alkoxy, -SR<sup>5</sup>, -OR<sup>5</sup>, N(R<sup>5</sup>)<sub>2</sub>, -SO<sub>2</sub>R<sup>5</sup>, and -SO<sub>2</sub>R<sup>a</sup>;

E is aryl or heteroaryl, wherein said aryl or heteroaryl group, which may be monocyclic or bicyclic, is optionally substituted on either the carbon or the heteroatom with one to five substituents independently selected from the group consisting of C<sub>1-6</sub> alkyl, haloalkyl, halo, keto, alkoxy, -SR<sup>5</sup>, -OR<sup>5</sup>, N(R<sup>5</sup>)<sub>2</sub>, -SO<sub>2</sub>R<sup>5</sup>, and -SO<sub>2</sub>R<sup>a</sup>;

5

Each G is independently C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkyloxy, aryl, heteroaryl, C<sub>3-8</sub> cycloalkyl, heterocyclyl, -O-, NR<sup>5</sup>, S(O)<sub>m</sub>, or carbonyl wherein said groups are optionally substituted on either the carbon or the heteroatom with one to five substituents independently selected from the group consisting of C<sub>1-6</sub> alkyl, halo, keto, haloalkyl, hydroxyalkyl, -OR<sup>5</sup>, -NHS(O)<sub>2</sub>R<sup>5</sup>, -SO<sub>m</sub>R<sup>5</sup>, -SO<sub>m</sub>N(R<sup>a</sup>)(R<sup>b</sup>), -C(R<sup>a</sup>)(R<sup>b</sup>)OH, , heterocyclyl, aryl or heteroaryl;

10

R<sup>5</sup> is hydrogen, C<sub>1-6</sub> alkyl, aryl, aryl(C<sub>1-4</sub>)alkyl, heteroaryl, heteroaryl(C<sub>1-4</sub>)alkyl, C<sub>3-8</sub>cycloalkyl, C<sub>3-8</sub>cycloalkyl(C<sub>1-4</sub>)alkyl, or heterocyclyl(C<sub>1-4</sub>)alkyl wherein said groups can be optionally substituted with one, two, or three substituents independently selected from the group consisting of halo, alkoxy, cyano, -NR<sup>a</sup> or -SR<sup>a</sup> or -SO<sub>m</sub>R<sup>5</sup>;

15

R<sup>a</sup> is hydrogen or C<sub>1-6</sub> alkyl which is optionally substituted with one, two, or three substituents independently selected from the group consisting of halo and -OR<sup>5</sup>;

R<sup>b</sup> is hydrogen or C<sub>1-6</sub> alkyl which is optionally substituted with one, two, or three substituents

20

independently selected from the group consisting of halo and -OR<sup>5</sup>;

or R<sup>a</sup> and R<sup>b</sup> can be taken together with the nitrogen atom to which they are attached or are between them to form a C<sub>3-8</sub> heterocyclyl ring which is optionally substituted with one or two substituents independently selected from the group consisting of C<sub>1-6</sub> alkyl, halo hydroxyalkyl, hydroxy, alkoxy and keto;

25

m is an integer from zero to two;

n is an integer from one to three;

or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivative thereof.

30

2. The compound of Claim 1 wherein R<sup>1</sup> and R<sup>2</sup> can be taken together with the carbon atom to which they are attached to form a C<sub>3-8</sub> cycloalkyl ring wherein said ring system is optionally substituted with one or two substituents selected from the group consisting of C<sub>1-6</sub> alkyl and halo.

35

3. The compound of Claim 2 wherein R<sup>3</sup> is C<sub>1-6</sub> alkyl which is optionally substituted with one to six halo.

4. The compound of Claim 3 wherein R<sup>3</sup> is n-propyl, isobutyl, 2-fluoro-2-methylpropyl, 2-trifluoromethylpropyl, 3-fluoro-2-(2-fluoromethyl)propyl, 2,2-difluoroethyl, 2,2-difluoropropyl, 3,3,3-trifluoropropyl, or 2,2-dichloroethyl.

5. The compound of Claim 2 wherein R<sup>4</sup> is difluoromethyl, 2,2-difluoroethyl, trifluoromethyl or 3,3,3,2,2-pentafluoroethyl.

6. The compound of Claim 5 wherein D is phenyl.

7. The compound of Claim 6 wherein E is phenyl or heteroaryl.

8. The compound of Claim 7 wherein each G is independently C<sub>1-6</sub> alkyl, C<sub>3-8</sub> cycloalkyl or SO<sub>m</sub>CH(R<sup>a</sup>)(R<sup>b</sup>).

9. The compound of Claim 1 which is:

1-[4'-[(1S)-1-[[[(1S)-1-[(1-cyanocyclopropyl)amino]carbonyl]-3-fluoro-3-methylbutyl]amino]-2,2,2-trifluoroethyl][1,1'-biphenyl]-4-yl]-cyclopropanecarboxylic acid;

N<sup>1</sup>-(1-cyanocyclopropyl)-N<sup>2</sup>-{(1S)-2,2-difluoro-1-{4'-[1-(carboxy)cyclopropyl]biphenyl-4-yl}-ethyl}-L-leucinamide;

N<sup>1</sup>-(1-cyanocyclopropyl)-N<sup>2</sup>-{(1S)-2,2-difluoro-1-{4'-[1-(carboxy)cyclopropyl]biphenyl-4-yl}-ethyl}-4-fluoro-L-leucinamide;

1-[2-[4-[(1S)-1-[[[(1S)-1-[(1-cyanocyclopropyl)amino]carbonyl]-3-fluoro-3-methylbutyl]amino]-2,2,2-trifluoroethyl]phenyl]-4-thiazolyl]-cyclopropanecarboxylic acid;

1-[[4'-[(1S)-1-[[[(1S)-1-[(1-cyanocyclopropyl)amino]carbonyl]-3-methylbutyl]amino]-2,2-difluoroethyl][1,1'-biphenyl]-3-yl]methyl]-cyclobutanecarboxylic acid;

4'-[(1S)-1-[[[(1S)-1-[(1-cyanocyclopropyl)amino]carbonyl]-3-fluoro-3-methylbutyl]amino]-2,2,2-trifluoroethyl]-α,α-dimethyl-[1,1'-biphenyl]-4-propanoic acid;

1-[4'-[(1*S*)-1-[[[(1*S*)-1-[(1-cyanocyclopropyl)amino]carbonyl]-3-methylbutyl]amino]-2,2,2-trifluoroethyl][1,1'-biphenyl]-4-yl]-cyclopropanecarboxylic acid;

5 1-[4'-[(1*S*)-1-[[[(1*S*)-1-[(1-cyanocyclopropyl)amino]carbonyl]-3-fluoro-3-methylbutyl]amino]-2,2,2-trifluoroethyl][1,1'-biphenyl]-3-yl]-cyclopropanecarboxylic acid;

4'-[(1*S*)-1-[[[(1*S*)-1-[(1-cyanocyclopropyl)amino]carbonyl]-3-fluoro-3-methylbutyl]amino]-2,2,2-trifluoroethyl]- $\alpha$ -methyl-[1,1'-biphenyl]-4-acetic acid;

10 4'-[(1*S*)-1-[[[(1*S*)-1-[(1-cyanocyclopropyl)amino]carbonyl]-3-fluoro-3-methylbutyl]amino]-2,2,2-trifluoroethyl]- $\alpha,\alpha$ -dimethyl-[1,1'-biphenyl]-4-acetic acid;

15 1-[4'-[(1*S*)-1-[[[(1*S*)-1-[(1-cyanocyclopropyl)amino]carbonyl]-3-fluoro-3-methylbutyl]amino]-2,2,2-trifluoroethyl][1,1'-biphenyl]-4-yl]-cyclopropaneacetic acid;

1-[4'-[(1*S*)-1-[[[(1*S*)-1-[(1-cyanocyclopropyl)amino]carbonyl]-3-methylbutyl]amino]-2,2,2-trifluoroethyl][1,1'-biphenyl]-4-yl]-cyclopropanecarboxylic acid;

20 1-[4'-[(1*S*)-1-[[[(1*S*)-1-[(1-cyanocyclopropyl)amino]carbonyl]butyl]amino]-2,2,2-trifluoroethyl][1,1'-biphenyl]-4-yl]-cyclopropanecarboxylic acid;

4'-[(1*S*)-1-[[[(1*S*)-1-[(1-cyanocyclopropyl)amino]carbonyl]-3-fluoro-3-methylbutyl]amino]-2,2,2-trifluoroethyl]-[1,1'-biphenyl]-4-acetic acid;

25 *N*<sup>1</sup>-(1-cyanocyclopropyl)-4-fluoro-*N*<sup>2</sup>-((1*S*)-2,2,2-trifluoro-1-{4'-[(1*S*)-1-carboxyethyl]biphenyl-4-yl}-ethyl)-L-leucinamide;

or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivatives thereof.

30 10. A pharmaceutical composition comprising a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivatives thereof, and a pharmaceutically carrier.

11. The use of a compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivatives thereof, in the preparation of a medicament useful for the treatment of: osteoporosis, glucocorticoid induced osteoporosis, Paget's disease, abnormally increased bone turnover, periodontal disease, tooth loss, bone fractures, rheumatoid arthritis, osteoarthritis, periprosthetic osteolysis, osteogenesis imperfecta, atherosclerosis, obesity, chronic obstructive pulmonary disease, metastatic bone disease, hypercalcemia of malignancy or multiple myeloma in a mammal in need thereof a therapeutically effective amount of a compound according to Claim 1.

12. A pharmaceutical composition comprising a compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivatives thereof, and another agent selected from the group consisting of: an organic bisphosphonate, an estrogen receptor modulator, an estrogen receptor beta modulator, an androgen receptor modulator, an inhibitor of osteoclast proton ATPase, an inhibitor of HMG-CoA reductase, an integrin receptor antagonist, or an osteoblast anabolic agent, a Nonsteroidal anti-inflammatory drug, a selective cyclooxygenase-2 inhibitor, an inhibitor of interleukin-1 beta, a LOX/COX inhibitor and the pharmaceutically acceptable salts and mixtures thereof.

13. The use of a compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivatives thereof, and another agent selected from the group consisting of: an organic bisphosphonate, an estrogen receptor modulator, an androgen receptor modulator, an inhibitor of osteoclast proton ATPase, an inhibitor of HMG-CoA reductase, an integrin receptor antagonist, an osteoblast anabolic agent, a Nonsteroidal anti-inflammatory drug, a selective cyclooxygenase-2 inhibitor, an inhibitor of interleukin-1 beta, a LOX/COX inhibitor and the pharmaceutically acceptable salts and mixtures thereof, in the preparation of a medicament useful for the treatment of: osteoporosis, glucocorticoid induced osteoporosis, Paget's disease, abnormally increased bone turnover, periodontal disease, tooth loss, bone fractures, rheumatoid arthritis, osteoarthritis, periprosthetic osteolysis, osteogenesis imperfecta, atherosclerosis, obesity, chronic obstructive pulmonary disease, metastatic bone disease, hypercalcemia of malignancy or multiple myeloma in a mammal in need thereof.